

AR201-1400A

NCIC Received 10/8/02
10:36 AM

High Production Volume (HPV) Challenge Program

Test Plan and Robust Summaries

For

n-Butyl Glycidyl Ether

Submitted to the US Environmental Protection Agency

by

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**Revised Submission: September 2002
Original Submission: December 2001**

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LIST OF REFERENCES

ROBUST SUMMARIES

1.0 INTRODUCTION

n-Butyl glycidyl ether (BGE; CAS # 2426-08-6) is an epoxy resin additive derived from glycidol employed in coatings, electronics, structural composites and adhesives. The Environmental Protection Agency (EPA) defines the chemical category, glycidyls, as all substances with the general formula:



where R is a hydrogen atom or any alkyl, aryl, or acyl group, and R is unrestricted as to the number and type of substituents it may carry.

The Epoxy Resin Systems Task Group (ERSTG) of The Society of the Plastics Industry, Inc. (SPI) has committed to provide basic physical chemistry, environmental fate, ecotoxicity, and health effects information on n-butyl glycidyl ether listed under the Environmental Protection Agency (EPA) High Production Volume (HPV) Chemical Challenge Program. By participating in this voluntary program, the ERSTG agreed to assess the adequacy of existing data; prepare summaries of the data characterizing the chemical; determine data needed to fulfill HPV data requirements; and design and submit a test plan to satisfy these testing requirements.

The HPV Challenge Program endorses the development of chemical categories and the use of surrogate data from a structurally similar chemical(s) as an acceptable mechanism to achieve an efficient completion of the program goals. EPA considers this an acceptable premise for chemicals whose physicochemical and toxicological properties are likely to be similar or follow a regular pattern as a result of structural similarity. The ERSTG believes t-butyl glycidyl ether (CAS # 7665-72-7) has similar physicochemical and toxicological properties, and is therefore an acceptable surrogate source of data in support of n-butyl glycidyl ether under the HPV Challenge Program.

n-Butyl glycidyl ether is a mono-epoxy functional glycidyl ether where the R group is a straight chain butyl. This compound has a viscosity of 0-2 cP at 25 degrees C, specific gravity of 0.92-0.94 and a flash point of 132 degrees F. A comparison between n-butyl glycidyl ether and t-butyl glycidyl ether shows the following:

	<u>n-Butyl</u>	<u>t-Butyl</u>
Molecular Weight	130	130
Boiling Point (°C)	164	152
Density	0.908	0.917
Solubility	2 g/100 ml	1-5 g/100 ml
Physical Appearance	liquid (clear)	liquid (clear)

While the tertiary butyl alignment may present some steric hindrance, the functional groups (ethers) must be very similar in reaction. Lindbohn and Wallgren (1962) note “the effects of n-butyl and t-butyl alcohol on the respiration of electrically stimulated and unstimulated

slices of rat brain cortical tissue were studied. n-Butyl alcohol, at a concentration of 9mM, and t-butyl alcohol, at a concentration of 41 mM, reduced the respiration of stimulated tissue by about 11.5%”[Ref 14]. Although n-butyl alcohol is more readily metabolized to the end carbon, the difference between the n- and t- butyl alcohols is only a factor of 4. Further support for their similar biological activity can be found in the American Conference of Governmental Industrial Hygienists (ACGIH) discussion of the Threshold Limit Value (TLV) (1986): “signs of intoxication in animals exposed to vapors of t-butyl alcohol are similar to those of the other butyl alcohols”[Refs 17 and 18]. Examination of the totality of data for n- and t-butyl glycidyl ether demonstrates that they share similar toxicity at comparable dose levels. For example: (1) the acute oral LD50 was 1-2 gm/kg, (2) the subchronic inhalation effects after 14-28 days were primarily body weight reduction at 0.1 – 0.5 mg/L, and (3) the mutagenic effects in the Ames assays, Micronucleus assays, and Dominant Lethal assays were all similar. The n-butyl glycidyl ether studies illustrate similarities to t-butyl glycidyl ether in effects observed at comparable dose levels, NOAELs, and positive/negative responses in a battery of mutagenicity studies.

2.0 EVALUATION OF DATA

Where data are lacking for the HPV chemical, n-butyl glycidyl ether, use of data from the surrogate chemical, t-butyl glycidyl ether, is not only scientifically justified, but also encouraged. This position is bolstered by: (1) EPA’s guidance on the category approach noted above under 1.0; and (2) its position presented before the Organisation for Economic Co-operation and Development (OECD) Working Party on Existing Chemicals (1999) that industry should minimize, as well as optimize, animal usage when fulfilling HPV data requirements. Therefore, data for both CAS # 2426-08-6 and 7665-72-7 have been considered equally with regards to HPV data requirements for CAS #2426-08-6, using scientifically reliable data. A table showing the available studies for the HPV endpoints is located on page 7.

2.1 Physical Chemical Description of n-Butyl Glycidyl Ether

2.1.1 Melting Point: –30.96°C [Ref 20]

2.1.2 Boiling Point: 164°C [Ref 15]

2.1.3 Vapor Pressure: 3.2 mmHg @ 25°C [Ref 15]

2.1.4 Partition Coefficient: Log Kow = 0.63 [Ref 19]

2.1.5 Water Solubility: 2 g/100 ml @ 20°C [Ref 16]

2.1.6 Summary of Physical Chemical Data

Data are available for all physical chemical endpoints; no further testing is proposed.

2.2 Environmental Fate and Pathways Data

2.2.1 Biodegradation

n-Butyl glycidyl ether oxidized to 25% of the theoretical oxygen demand by day 28 in a closed bottle test (OECD 301D) and 4-12% degradation compared to theoretically possible carbon dioxide in the Modified Sturm test (OECD 301B). These tests indicate that n-butyl glycidyl ether is partially biodegradable to having “no evidence of biodegradability,” respectively. [Ref. (9)]

2.2.2 Photodegradation

Estimation Programs Interface for Microsoft® Windows (EPIWIN V3.05, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D.C.), Atmospheric Oxidation Program (v1.90) modeling component was used to calculate the rate of photodegradation for n-butyl glycidyl ether. The half-life was calculated to be 0.539 days (or 6.466 hours), assuming the reaction occurred over a 12-hour day with an average atmospheric concentration of $1.5E6 \text{ OH/cm}^3$ [Ref. (21)].

2.2.3 Hydrolysis (Stability in Water)

No data available; testing is proposed to determine stability in water.

2.2.4 Transport/Distribution

The LEV3EPI fugacity model (from EPIWIN V3.05, USEPA) was used for predicting partitioning of n-butyl glycidyl ether among air, water, soil and sediment compartments. The following are the concentration results using a soil K_{oc} of 1.75 as calculated by the model and a log K_{ow} of 0.63 [Ref. (19)]:

- Air 2.7%
- Water 53.5%
- Soil 43.8%
- Sediment <0.1%

2.2.5 Summary of Environmental Fate and Pathways Data

Testing is proposed to determine stability in water.

2.3 Ecotoxicology Data

2.3.1 Acute Toxicity to Fish

Rainbow trout were exposed for 96 hours to five different concentrations of n-butyl glycidyl ether ranging from 10 to 200 mg/L. The 96-hour LC50 was 65 mg/L, indicating that it is harmful to rainbow trout. [Ref. (10)]

2.3.2 Acute Toxicity to Aquatic Invertebrates

In a 48-hour static test, 100 ml of test medium (consisting of reconstituted fresh water) was added to 150-ml glass dishes. n-Butyl glycidyl ether was then added to the dishes to give log series concentrations ranging from 1 to 1000 mg/L. Daphnia magna less than 24 hours old were added to each dish and after 24 and 48 hours the number of immobilized Daphnia were counted. The 24- and 48-hour EC50s were 22 and 3.9 mg/L, respectively. [Ref. (12)]

In a separate study, Pacific Oysters (Crassostrea gigas) were examined to determine the ability of embryos to develop into shelled D-stage veligers within 24 hours. Tests were performed in artificial seawater. The oysters were conditioned to a pre-spawning state by maintaining them in recirculating sea water at a temperature of 25°C and fed a mixed algae diet. Detailed procedures were provided on embryo preparation, estimating egg

and embryo density and fertilization of embryos. Exposure was completed by adjusting the density of an embryo suspension by dilution with seawater and inoculation into 30-ml glass bottles containing test media. Test concentrations of n-butyl glycidyl ether ranged from 18 to 190 mg/L. Test vessels were incubated for 24 hours at 25°C with artificial lighting providing a 16-hour light and 8-hour dark cycle. The percent abnormality at each test concentration was calculated and Percent Net Response (PNR) was determined. The PNR was used to calculate a 24-hour EC50, which was 74 mg/L. [Ref. (13)]

Test results from both invertebrate species demonstrate that n-butyl glycidyl ether ranges from harmful to toxic to aquatic invertebrates.

2.3.3 Toxicity to Aquatic Plants

Fresh water green algae, Selenastrum capricornutum, were examined in a 4-day growth inhibition test. Eighteen flasks containing 50 ml of culture medium were prepared. n-Butyl glycidyl ether was added to 12 of these flasks to give log concentrations ranging from 10 to 300 mg/L. The remaining 6 flasks served as controls. Each flask was inoculated to give an initial cell concentration of 5×10^3 cells/ml. Flasks were incubated under constant light at 24°C for 4 days. The mean relative growth rate (RGR) from each culture was calculated, and the EC50 value (concentration causing 50% reduction in RGR) was determined. The 96-hour EC50 was 35 mg/L, indicating n-butyl glycidyl ether is harmful to aquatic plants. [Ref. (11)]

2.3.4 Summary of Ecotoxicology Data

n-Butyl glycidyl ether demonstrated that it is harmful to fish and aquatic plants, and that it ranges from harmful to highly toxic to aquatic invertebrates. Studies in aquatic plants, acute toxicity testing in fish, and testing in invertebrate species are scientifically reliable and no further ecotoxicology testing is proposed.

2.4. Health Effects Data

2.4.1 Acute Health Effects

2.4.1.1 Acute Oral Toxicity

In an acute oral toxicity study, male rats were given a single dose of undiluted t-butyl glycidyl ether via gastric intubation. Five doses were administered, ranging from 0.126 to 2 g/kg body weight. All animals were weighed prior to dosing and at weekly intervals until study termination 2 weeks post-dosing. One rat per dose was subjected to gross necropsy. There were no adverse effects observed, no effect on body weight gain, no gross pathological changes, and no mortality at the 3 lowest doses. At 1 g/kg there was slight accumulation of darkened material around the external nares and the mucosal surface of the stomach was slightly edematous. At 2 g/kg, one rat died and the effects observed were the same as those observed at 1 g/kg. [Ref. (1)] Two other published reports, support an acute oral LD50 in rats of >2 g/kg. The first, published in 1963, indicates an LD50 of 2.05 (1.56-2.69) g/kg for rats. [Ref. 23] The second provides an LD50 of 2.26 g/kg (rat, intragastric), and an LD50 of 1.53 (1.17-2.0) g/kg for mice (intragastric). [Ref. 24]

2.4.1.2 Summary of Acute Toxicological Effects

A scientifically reliable acute oral toxicity study performed using t-butyl glycidyl ether demonstrates that the test material is not highly toxic and no further testing is proposed.

2.4.2 Genetic Toxicology

2.4.2.1 Bacterial Gene Mutation Assay

n-Butyl glycidyl ether was examined for gene mutations in the Ames Salmonella typhimurium assay and was positive in both the TA 100 and TA1535 strains, both with and without metabolic activation. [Ref. 5].

2.4.2.2 In Vitro Mammalian Cell Gene Mutation Assay

n-Butyl glycidyl ether was examined for gene mutations in mammalian cells in culture in the mouse lymphoma assay, using L5178Y heterozygous for TK+/- . n-Butyl glycidyl ether was tested in this forward mutation assay at concentrations ranging from 84 to 800 µg/ml, with and without Aroclor 1254 induced rat liver S9 metabolic activation. n-Butyl glycidyl ether was positive in the test system with and without metabolic activation. [Ref. (6)]

2.4.2.3 In Vivo Chromosomal Aberration Assay

n-Butyl glycidyl ether was examined for chromosomal aberrations in mice, in a dominant lethal assay, and produced equivocal results at 1.5 g/kg, the highest dose tested in this assay [Ref. 7]. However, in a previous study (Klimisch Rating of 3), n-butyl glycidyl ether of unknown purity produced positive dominant lethal effects at 1.5 and 3.0 g/kg. It is concluded that n-butyl glycidyl ether produced equivocal/ positive results in the dominant lethal assay. An in vitro chromosomal aberration test, conducted according to OECD guidelines, is proposed.

2.4.2.4 Unscheduled DNA Synthesis

n-Butyl glycidyl ether was evaluated in an unscheduled DNA repair assay by monitoring [³H] thymidine incorporation into DNA of G₀ phase cells of the human cell line, WI38. Doses ranged from 0.24 to 1.2 µl/ml (with S9 activation) and 0.5 to 8 µl/ml (without activation). WI38 was incubated with test material in DMSO for 3 hours. 0.1 ml of the DNA solution was used to measure DNA content after reacting with diphenylamine and a second aliquot used to determine incorporation of ³H-TdR (tritium labeled thymidine) by scintillation counting. Results were the average of 6 replicate samples. The results demonstrated that n-butyl glycidyl ether was not mutagenic in this test system. This is not an HPV data requirement for examining genetic effects. [Ref. (8)]

2.4.2.5 Summary of Genetic Toxicology Effects

n-Butyl glycidyl ether was examined for gene mutation effects in both an in vitro Ames assay and an in vitro mammalian cell assay, with and without metabolic activation. It was positive in both assays for gene mutations. These studies are considered scientifically reliable and satisfy the HPV data requirement for an in vitro gene mutation assay. In an unscheduled DNA repair assay, n-butyl glycidyl ether was negative. In a Dominant

Lethal assay in mice, n-butyl glycidyl ether produced equivocal/positive results. This study is considered scientifically reliable, but may not satisfy the HPV data requirement for a chromosome aberration assay. Based upon all of the data reviewed, it is concluded that n-butyl glycidyl ether produced positive responses in in vitro gene mutation assays, and equivocal results in an in vivo chromosome assay. An in vitro chromosomal aberration test, conducted according to OECD guidelines, is proposed.

2.4.3 Repeated Dose Health Effects

2.4.3.1 Subchronic Inhalation Toxicity

2-Week Inhalation Toxicity Study: Inhalation exposures of rabbits, rats and mice to t-butyl glycidyl ether were conducted in 4.1 m³ stainless steel and glass chambers under dynamic air flow conditions. Exposure concentrations ranged from 100 to 1000 ppm (equivalent to 0.52 to 5.2 mg/L). Animals were exposed 6 hours per day, 5 days/week for 2 weeks. Cageside observations revealed rhinitis, lethargy and gait changes in all species. All rabbits and 4/6 female mice died at 1000 ppm. Mean body weight decreases were measured at 300 ppm and 1000 ppm in all animals, but no effects were observed at 100 ppm. There were no effects on hematology, clinical chemistry or urinalysis at 100 or 300 ppm. Effects at 1000 ppm were not deemed interpretable due to the debilitated condition of all animals. Absolute and relative organ weight measurements for liver, kidney, brain, heart, thymus and testes were normal except for decreased liver weights at 300 ppm. Gross pathological examinations revealed treatment related effects at 300 and 1000 ppm in all species, primarily confined to decreased body fat, thymus, and lymphoid organs. Corneal cloudiness was observed in rats. A No Observable Adverse Effect Level (NOAEL) of 100 ppm was demonstrated, based on body weight changes and debilitated condition at 300 ppm and above. [Ref. (2)]

90-Day Repeated Dose Inhalation Toxicity Study: Inhalation exposures of rabbits, rats and mice to t-butyl glycidyl ether were conducted in 4.3 m³ stainless steel and glass chambers under dynamic air flow conditions. Exposure concentrations ranged from 25 to 225 ppm (equivalent to 0.13 to 1.19 mg/L). Animals were exposed 6 hours per day, 5 days/week for 13 weeks. Cageside observations conducted daily were unremarkable. Body weight gains were decreased in all species at 225 ppm, and in mice at 75 ppm. There were no compound-related effects on hematological, clinical chemistry, or urinalysis parameters measured. Absolute and relative organ weights were determined for liver, kidneys, brain, heart, thymus and testes. There were decreased liver weights in female rats and mice at 75 and 225 ppm. A full compliment of tissues were fixed and examined grossly, including all reproductive organs, in all dose groups. All species displayed decreased body fat and thymic size at 225 ppm. In addition, rabbits had atelectasis of the lung at 75 and 225 ppm. No gross adverse effects were observed in any of the reproductive organs/tissues examined. Histopathological examination of all tissues revealed the primary effect in all species confined to the respiratory system: thickening or flattening of olfactory epithelium in nasal turbinates, subepithelial inflammatory cell infiltrate, with hyperplasia in respiratory epithelium at higher doses. These effects occurred at 75 and 225 ppm. Also, decreased size of hepatocytes was observed, mostly at upper doses, but it did occur in mice and rabbits at 25 ppm. No changes in any reproductive organ or tissue were observed. The authors concluded that a NOAEL was

demonstrated at 25 ppm, based upon effects on the respiratory system, and organ weight changes at 75 and 225 ppm. However, based on the decreased hepatocyte size in mice and rabbits at 25 ppm, and the occurrence of atelectasis in rabbits at 25 ppm, 25 ppm is suggested as a LOAEL for these species with 25 ppm remaining the NOAEL for rats. [Ref. (3)]

Repeated inhalation exposures to t-butyl glycidyl ether for up to 13 weeks primarily affected the respiratory tract and epithelial lining of the nasal turbinates in rabbits, rat and mice. Also, repeated exposures caused body weight decreases, decreases in thymic size and debilitated condition at upper doses. There were no adverse effects on the reproductive organs in males and females examined grossly or histologically at doses up to and including 225 ppm. The NOAEL in all three species for repeated inhalation exposures to t-butyl glycidyl ether for two weeks was 100 ppm and the NOAEL for repeated inhalation exposures for thirteen weeks was 25 ppm.

Based upon the data generated from these repeated dose studies under Good Laboratory Practice (GLP) regulations, in accordance with recognized national and international scientific procedures, there are no additional repeated dose studies needed.

2.4.4 Reproductive Toxicity

Effects on the reproductive organs were assessed in the repeated dose inhalation toxicity studies summarized above. The male reproductive organs were examined grossly and histologically in the 2-week inhalation study and no adverse effects were observed at any dose. In the 90-day repeated dose inhalation study, male and female reproductive organs/tissues were examined in three species. Absolute and relative organ weights were normal. Gross and histopathological examinations were also normal with respect to concurrent controls in all dose groups up to and including 225 ppm (high dose). In male rats and mice, the following organs/tissues were examined: testes, epididymides, prostate, seminal vesicles, coagulating gland and preputial gland (rat only). In male rabbits only the testes, epididymides and accessory sex glands were examined. In females (all species), ovaries, oviducts, uterine horn, cervix, and vagina were examined. [Ref. (2) and (3)]

Based upon the extensive examination of reproductive organs in these studies, no further testing for reproductive effects is considered necessary. This conclusion is also supported by guidance presented in EPA's guidance document for meeting HPV requirements wherein it is recommended that if you have an adequate 90-day study that looks at reproductive organs, then a separate reproductive toxicity study is not necessary.

2.4.5 Developmental Toxicity

There were no developmental toxicity data available. An appropriate developmental toxicity test is proposed.

2.4.6 Summary of Repeated Dose, Reproductive and Developmental Toxicity Effects

All of the repeated dose toxicity studies were performed using t-butyl glycidyl ether. All studies are considered scientifically reliable and support the findings with respect to NOAELs and compound-related effects observed. Repeated inhalation exposures for 2 weeks or 13 weeks did not cause adverse effects to any organ system at 100 or 25 ppm, respectively. Primary effects were confined to the respiratory tract and epithelial lining of nasal turbinates. Also, repeated exposures caused body weight decreases, decreases in thymic size and debilitated condition at upper doses.

Effects on the reproductive organs were assessed in the repeated dose studies summarized above. There were no adverse effects on the reproductive organs in males and females examined grossly or histologically at doses up to and including 225 ppm.

All of these studies are scientifically reliable, comply with GLP regulations and were conducted according to international standards for such studies. No further testing is necessary, except for a developmental toxicity study.

3.0 CONCLUSIONS

The following table identifies the data available and the HPV data requirements that exist for n-butyl glycidyl ether. Scientifically reliable data exist for most of the HPV endpoints. Stability in water (hydrolysis) data is not available; testing is proposed. Further, examination of available data for health effects demonstrated that a developmental toxicity study conducted in accordance with OECD test guidelines is proposed.

TABLE 1: HPV DATA REQUIREMENTS/CRITICAL STUDIES: n-Butyl Glycidyl Ether

HPV Data Category	Test Endpoint		Data Acceptable	Data to be Generated
Physical and Chemical Properties	Melting Point		Yes	No
	Boiling Point		Yes	No
	Vapor Pressure		Yes	No
	Partition Coefficient		Yes	No
	Water Solubility		Yes	No
Environmental Fate and Pathways	Photodegradation		PD-1 (2)	No
	Stability in Water		ND	Yes
	Biodegradation		B-1 (1)	No
	Transport/Distribution		TD-1 (2)	No
Ecotoxicity	Acute toxicity to fish		AF-1 (2)	No
	Acute toxicity to aquatic invertebrates		ADP-2 (1) and AINV-1 (1)	No
	Toxicity to aquatic plants		AL-1 (1)	No
	Chronic aquatic ¹ invertebrate test		NR	No
	Terrestrial toxicity ¹		NR	No
Health Effects	Acute toxicity		AO-1 (2), AO-2(4), and AO-3 (4) <u>SU</u>	No
	Repeated Dose		SC-1 (1) and SC-2 (1) <u>SU</u>	No
	Genetic Toxicity	Gene Mutation	MU-13 (2), MU-14 (2) and MU-15 (2)	No
		Chromosome Aberration	MU-7 (2)	Yes
	Reproductive Toxicity		SC-2 (1) <u>SU</u>	No
	Developmental Toxicity		ND	Yes

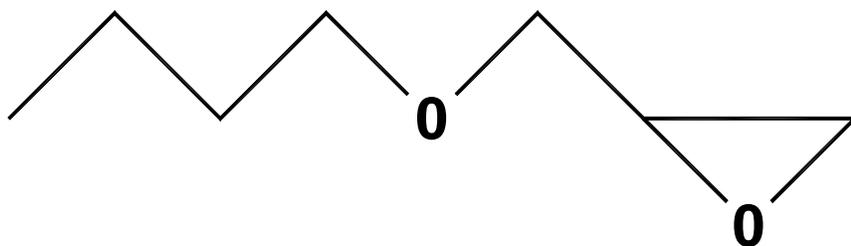
¹ = Tests are not required for all chemicals; only when appropriate. NR = Not required

ND = No data

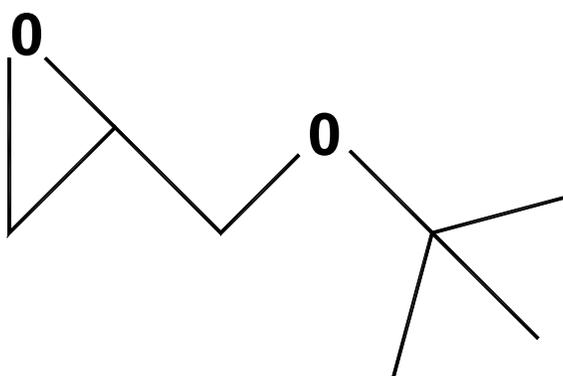
SU = Surrogate Data from t-butyl glycidyl ether.

Data listed are cross-referenced to a Robust Summary report number (i.e. AO-1 (2)); which identifies the report number followed by the Klimisch Rating in (). Only studies with the following Klimisch Ratings are included: (1) = reliable without restriction and (2) = reliable with restriction. If this is followed by SU, it means the critical study was derived from surrogate data (i.e. t-butyl glycidyl ether). If more than one study is listed it means they are co-critical.

n-Butyl Glycidyl Ether
[2426-08-6]



tert-Butyl Glycidyl Ether
[7665-72-7]



LIST OF REFERENCES

7665-72-7 (t-Butyl Glycidyl Ether)

Ref. (1). AO-1(t): Acute Oral

Dow Chemical USA. Toxicological Properties and Industrial Handling Hazards of 1-Tertiary-Butoxy-2,3-epoxy Propane. Testing Facility: Chemical Biology Research, Dow Chemical Company, Midland, MI; Study #T36.1-59376-2; Study dated March 1972.

Klimisch = 2

Ref. (2). SC-1(t): Repeated Dose

Dow Chemical USA. T-Butyl Glycidyl Ether (TBGE): A 2-Week Inhalation Study in Rabbits, Rats, and Mice. Testing Facility: Toxicology Research Laboratory, Health & Environmental Sciences, USA, Dow Chemical USA, Midland, MI; Study #K-59376-(6); Study dated March 1984.

Klimisch = 1

Ref. (3). SC-2(t): Repeated Dose and Reproduction

Dow Chemical USA. T-Butyl Glycidyl Ether (TBGE): 90-Day Inhalation Study in Rats, Mice and Rabbits. Testing Facility: Toxicology Research Laboratory, Health & Environmental Sciences, USA, Dow Chemical USA, Midland, MI; Study #K-59376-(7); Study dated May, 1984.

Klimisch = 1

Ref (15). Boiling Point and Vapor Pressure

Sax, N.I. and R.J. Lewis, Sr (eds). Hawley's Condensed Chemical Dictionary. 11th ed. New York: Van Nostrand Reinhold Co., 1987.

Klimisch = 2

Ref (16). Water Solubility

Patty, F. (ed). Industrial Hygiene and Toxicology: Volume II: Toxicology. 2nd ed. New York: Interscience Publishers, 1963. Pg 1604.

Klimisch = 2

Ref (19). Octanol Water Partition Coefficient

Hansch, C., Leo, A., D. Hoekman. Exploring OSAR – Hydrophobic, Electronic and Steric Constants. Washington, D.C., American Chemical Society, 1995; 35.

Klimisch = 2

2426-08-6 (n-Butyl Glycidyl Ether)

Ref. (4). DS-4(n)

Dow Chemical USA. A Series of Guinea Pig Sensitization Tests for Structure-Activity Correlation – Epoxides. Testing Facility: Mammalian and Environmental Toxicology Laboratory, Health & Environmental Sciences, USA, Dow Chemical USA, Midland, MI; Study #HET T2.2-173-003; Study dated May, 1986.

Klimisch = 2

Ref. (5). MU-13(n): In Vitro (Gene Mutation: Bacteria Cells)

The Proctor and Gamble Company. Mutagenicity of Alkyl Glycidyl Ethers in Three Short-Term Assays. Testing Facility: Miami Valley Laboratories, Cincinnati, OH; Hazleton Laboratories of America, Vienna, VA and SRI International, Menlo Park, CA; Study – Published report by Proctor and Gamble in Mutation Research, 90:213-231(1981); Study dated June, 1981.

Klimisch = 2

Ref. (6). MU-14(n): In Vitro (Gene Mutation: Mammalian Cell)

The Proctor and Gamble Company. Mutagenicity of Alkyl Glycidyl Ethers in Three Short-Term Assays. Testing Facility: Miami Valley Laboratories, Cincinnati, OH; Hazleton Laboratories of America, Vienna, VA and SRI International, Menlo Park, CA; Study – Published report by Proctor and Gamble in Mutation Research, 90:213-231(1981); Study dated June, 1981.

Klimisch = 2

Ref. (7). MU-7(n): In Vivo Chromosomal Aberration Assay

Dominant Lethal Effects of n-butyl glycidyl ether in Mice. Whorton, Pullin, Frost, Onofre, Legator and Folse; Mutation Research, 124:225-233 (1983).

Klimisch = 2

Ref. (8). MU-15(n): Genetic Toxicity: UDS

The Proctor and Gamble Company. Mutagenicity of Alkyl Glycidyl Ethers in Three Short-Term Assays. Testing Facility: Miami Valley Laboratories, Cincinnati, OH; Hazleton Laboratories of America, Vienna, VA and SRI International, Menlo Park, CA; Study – Published report by Proctor and Gamble in Mutation Research, 90:213-231(1981); Study dated June, 1981.

Klimisch = 2

Ref. (9). B-1: Biodegradation

SICC/CSAS. n-Butylglycidyl Ether: Assessment of Ready Biodegradability. Testing Facility: Shell Biosciences Laboratory, Sittingbourne Research Center; Study #ST80/056 SBGR.82.069; Study dated 1981.

Klimisch = 1

Ref. (10). AF-1: Aquatic Toxicity: Fish

SICC/CSAS; Shell Oil Company. N-Butylglycidyl Ether Acute Toxicity to *Salmo gairdneri*. Testing Facility: Shell Toxicology Laboratory (Tunstall), Sittingbourne Research Center, Kent England; Study #SBGR.82.148; Study dated Apr. 1982.

Klimisch = 2

Ref. (11). AL-1: Aquatic Toxicity

SICC/CSAS, Shell Oil Company. N-Butylglycidyl Ether Acute Toxicity to *Salmo gairdneri*, *Daphnia magna* and *Selenastrum capricornutum*. Testing Facility: Shell Toxicology Laboratory (Tunstall), Sittingbourne Research Center, Kent England; Study #SBGR.82.148; Study dated 1982.

Klimisch = 1

Ref. (12). ADP-2: Aquatic Toxicity: Invertebrates

SIRM, RS, Shell Oil Company. Toxicity Tests with Daphnia magna: Acute Toxicity of Eight Test Materials to a Newly-Introduced Strain of D. magna in Reconstituted Fresh Water. Testing Facility: Shell Toxicology Laboratory (Tunstall), Sittingbourne Research Center, Kent England; Study #SBGR.83.100; Study dated 1983.

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Ref. (13). AINV-1: Aquatic Toxicity: Invertebrates

SIRM, RS, Shell Oil Company. Evaluation of the Pacific Oyster (Crassostrea gigas) Embryo Larval Test: Statistical Validation of the Test Procedure and Susceptibility to Reference Toxicants. Testing Facility: Shell Toxicology Laboratory (Tunstall), Sittingbourne Research Center; Study #SRC37992; Study dated 1992.

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Ref. (20). Melting Point

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Klimisch = 2

Ref (21). PD-1: Photodegradation

Estimation Programs Interface for Microsoft® Windows (EPIWIN V3.05, U.S. Environmental Protection Agency, Office of Pollution Prevention and Toxics, Washington, D.C.)

Klimisch = 2

Ref (22). TD-1: Transport/Distribution

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Ref (23). AO-2: Acute Oral Toxicity in Rats

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